Attorney Docket No. O/98414 US

REMARKS

Claims 1-5 and 7 are pending in the instant application. Claim 1 is independent. Applicants have not raised any issues of new matter.

Issue Under 35 U.S.C. §103(a)

Claims 1-5 and 7 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lobaccaro et al. (J. Med. Chem., 1997, 40, 2217-2227). Applicants assert that patentable distinctions exist between the present invention and Lobaccaro et al.

Distinctions Between the Present Invention and Lobaccaro et al.

The Examiner asserts that compounds 5a-b in scheme 1 of Lobaccaro et al. render the present invention obvious because the alkyl chains at the 11 position are "substantially similar." The Examiner has asserted that the results shown in Example III on page 13-15 of the specification fails to show unexpected results; thus, the Examiner asserts that a skilled artisan would find a change from 4 carbons to 5 carbons obvious.

Applicants disagree with the Examiner's assertions. Compounds 5a and 5b in Scheme 1 of Lobaccaro et al have butenyl and vinyl at the 11 position. More importantly, Lobaccaro et al only discloses these compounds as intermediates in a synthetic

pathway. In Tables 1 and 2 of Lobaccaro et al, compound 5b is an agonist and to achieve an antagonist Lobaccaro et al have made derivatives with mesylate, tosylate, etc. "[I]t appears that the threshold which separates estrogenic from antiestrogenic compounds is rapidly reached when the size of the 11β-alkyl chain increases, with a threshold between C-2 and C-4." *See page 2223, left column, second paragraph.* Therefore, a skilled artisan would not be motivated to make a compound with carbon chain of 5 to 9 carbon atoms at position 11.

Applicants respectfully request withdrawal of the 35 U.S.C. §103(a) rejection.

Issue Under 35 U.S.C. §103(a)

Claims 1-5 and 7 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Napolitano et al. (J. Med. Chem., 1995, 38, 2774-2779). Applicants assert that patentable distinctions exist between the present invention and Napolitano et al.

Distinctions Between the Present Invention and Napolitano et al.

Napolitano et al. discloses that the 11β position of the steroid is substituted or unsubstituted short chain alkyl groups (less than five carbon atoms). In Table 1, page 2776, Napolitano et al exclusively recites alkyl chains of 2 to 4

carbons in length. However, the Examiner asserts that a skilled artisan would be motivated to extend the carbon chain and expect similar results. The specification in Tables A and B provide relevant data showing unexpected results between an alkyl chain of 4 carbons and an alkyl chain of 5 carbons. Applicants believe these unexpected results rebut any argument of obviousness because a skilled artisan would not have had a reasonable expectation of success of achieving the selectivity of the present invention. See below for a more detailed explanation of the unexpected results.

Applicants respectfully request withdrawal of the 35 U.S.C. §103(a) rejection.

Unexpected Results

In Table A, page 14 of the present specification, Applicants recite that compounds 3, 5, 6, 8 and 11, which are the present invention, are agonist at ER-α and antagonist at ER-β. Compounds 1, 2, 4, 7 and 9-10 are agonist at both ER-α and ER-β. Compounds 1, 2, 4, 7 and 9-10 represent the closest prior art, which is Napolitano et al. Compounds 4 and 5 only differ by one carbon in the side chain at position 11, yet 4 is an

agonist ER-β and 5 is an antagonist at ER-β. The same can be said for the difference in compounds 10 and 11.

Applicants have claimed a series of compounds and a pharmaceutical composition that are agonist at ER-α and antagonist at ER-β. The cited prior art provides no motivation to make such compounds or compositions because a skilled artisan would not have had a reasonable expectation of success of making a series of compounds and a pharmaceutical composition that are agonist at ER-α and antagonist at ER-β from reading the cited prior art.

Applicants respectfully request withdrawal of the 35 U.S.C. §103(a) rejection.

Conclusion

Applicants submit that every issue raised by the outstanding Office Action has been addressed and rebutted. Therefore, the present claims define patentable subject matter and are in condition for allowance.

Should the Examiner believe that an Interview would be helpful in advancing the prosecution of this application, he is invited to telephone Applicants' Attorney at the number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or

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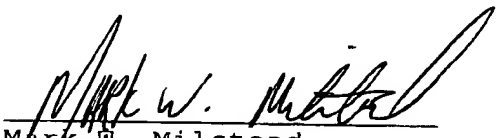
credit any overpayment to Deposit Account No. 02-2334 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,



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